detected in chondrogenic pellets and secreted by the differentiating MSCs. Finally, high levels of IL16 were detected in osteoarthritic cartilage.

Conclusions: We hypothesise that differentiation of MSCs initially involves hypermethylation to facilitate the rapid down regulatation of genes involved in self-renewal or alternative differentiation pathways. Epigenetic mechanisms also represent an important aspect of control to ensure the sequential and temporal expression of critical genes throughout the differentiation process. IL16, previously associated with synovial fibroblasts from rheumatoid joints was identified as a novel factor in chondrogenesis.

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NEUROMUSCULAR EXERCISE IMPROVES FUNCTIONAL PERFORMANCE IN PATIENTS WITH SEVERE HIP OSTEOARTHRITIS

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Purpose: Exercise is regarded a cornerstone in the treatment of mild to moderate osteoarthritis (OA). However, little is known of the effects in patients with advanced and end-stage OA. The purpose was to evaluate the effect of neuromuscular exercise in patients with severe hip OA.

Methods: *Design*. Randomized controlled trial (Clinicaltrials.gov identifier: NCT01003756). 84 patients, 51% female, mean age 68.6±7.8 years, BMI 28.7±4.7 scheduled for total hip replacement at Svendborg Community Hospital, Odense University Hospital, Denmark were included. *Intervention*. Participants were randomized to an eight-week neuromuscular exercise (NEMEX-TJR) intervention or care-as-usual (verbal and written preoperative information). Intervention was supervised and offered twice a week with each session lasting one hour. The program is considered feasible and safe in this patient group and previously described in detail. Assessments were carried out at baseline and within one week after the intervention. *Outcomes*. Functional performance: 20-m walk at maximal pace and 5 repeated chair stands timed. Muscle power: Unilateral multi-joint leg extension power and unilateral single-joint knee extension power evaluated with a leg extension press (Nottingham Power Rig, Nottingham University, Nottingham, UK) and a seated knee extension machine (Oemmebi, Moglia, Italy) adapted with a linear encoder (MuscleLab Power, Ergotest Technology, Langesund, Norway), respectively.

Results: On average the intervention group attended 13±4 sessions (Table 1). In favor of the intervention group, the between-group difference was significant for 20-m walk (2.2 seconds, p = 0.009), chair stands (1.7 seconds, p = 0.022) and leg extension for the non operated leg (.17 W/kg, p = 0.049) (Table 2).

Table 1. Baseline characteristics of study participants

	Exercise intervention	Care-as-usual
Scheduled for operation – no.	43	41
Female sex – no. (%)	22 (51)	21 (51)
Age – yr	68.7 [66.1;71.3]	68.6 [66.3;70.8]
BMI – kg m^{-2}	28.5 [27.3;29.7]	28.8 [27.1;30.5]
Exercise sessions – no.	13 [12.2;14.7]	–

Table 2. Baseline values and change over time (mean ± SD)

Outcome measure	Baseline		Change			
	Exercise intervention	Care-as-usual	Exercise intervention	Care-as-usual	Between-group mean difference	p-value
Muscle power (W kg^{-1})						
Multi-joint leg extension						
Non operated	1.28 [1.11;1.45]	1.33 [1.12;1.54]	0.22 [0.09;0.35]	0.05 [−.05;0.16]	0.17	0.049
Operated	1.02 [0.85;1.20]	1.09 [0.9;1.3]	0.07 [−0.07;0.20]	−0.05 [−0.18;0.08]	0.12	0.200
Single-joint knee extension						
Non operated	0.82 [0.67;0.96]	0.81 [0.65;0.97]	0.10 [0.05;0.16]	−0.01 [−0.14;0.11]	0.12	0.091
Operated	0.59 [0.47;0.72	0.58 [0.42;0.74	0.08 [0.01;0.14]	0.10 [−0.07;0.27]	0.03	0.761
Functional performance (s)						
Chair stands	13.1 [11.5;14.7]	13.4 [11.9;14.9]	−2.7 [−3.9;-1.4]	−0.5 [−1.6;0.7]	2.2	0.009
20-m max pace	15.2 [13.6;16.8]	15.6 [14.1;17.1]	−1.0 [−1.8;-.1]	0.7 [−0.5;1.9]	1.7	0.022

Conclusion: Eight weeks neuromuscular exercise according to the NEMEX-TJR program improves functional performance and leg extension power in patients with severe OA of the hip joint.

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TIME TO TOTAL HIP REPLACEMENT SURGERY AFTER SUPERVISED EXERCISE AND PATIENT EDUCATION IN PATIENTS WITH HIP OSTEOARTHRITIS. A RANDOMIZED INTERVENTION STUDY WITH BETWEEN 3.5 AND 6 YEARS FOLLOW UP

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Purpose: The purpose of the study was to evaluate time to total hip replacement (THR) surgery in patients with hip osteoarthritis going through both a supervised exercise program and patient education (SE+PE) compared to patients going through patient education only (PE).

Methods: One hundred and nine patients were included in the study between April 2005 and October 2007. Inclusion criteria were age 40–80 years, hip pain for three months or more, radiographically verified hip osteoarthritis (Danielson's criteria), and Harris Hip Score between 60–95 points, i.e. their impairments were not severe enough for considering THR at time of inclusion. All patients initially had three sessions of patient education. After completing the education program baseline assessments were conducted, and the patients were then randomized to 1) a 12 week supervised exercise program (SE+PE, n = 55), or 2) no further treatment (PE, n = 54). Both groups were recommended to follow the information giving during the patient education. The SE+PE group performed exercises 2–3 times weekly supervised by a physical therapist. The exercises consisted of strength training, functional exercises, and flexibility exercises.

Between April 12th and May 3rd 2011, 3.5 to 6 years after inclusion, all patients were contacted by telephone and information on whether and when THR surgery had been performed were collected. Survival analysis (Kaplan-Maier) were used to assess time to THR surgery in both groups. Group differences were tested by the Log Rank test.

Results: Twelve patients (11%) did not respond at latest follow-up (April/May 2011). Six of these patients had previously informed us that they had gone through THR surgery and at what time, and the remaining six patients were censored.

In total, 53 (48.6%) patients went through THR surgery within the follow-up time, 22 (40.0%) in the SE+PE group and 31 (57.4%) in the PE group. Median time to THR surgery was 1953 days (95% confidence interval (CI): 1634, 2272) and 1260 days (95% CI: 850, 1670) in the PE group. Cumulative survival without THR surgery after 6 years was 41.4% in the SE+PE group and 25.4% in the SE group (Figure 1, p = 0.034).

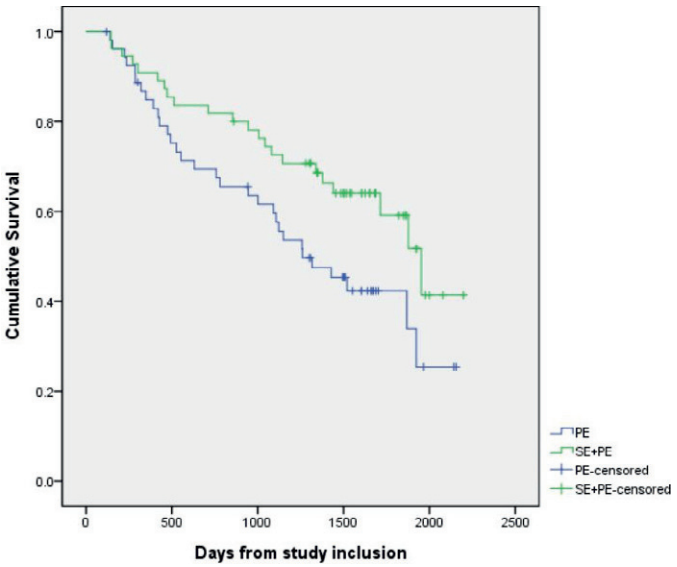

Fig. 1. Kaplan–Meier plot. Cumulative survival (without THR surgery) in the SE+PE group (green line) and the PE group (blue line). Censored data is marked at each line.